

CLAIMS

1. A substantially pure consecutive and anti-angiogenic polypeptide, comprising the central
5 region of human histidine rich glycoprotein (HRGP) corresponding to SEQ.ID.NO:2.
2. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment
corresponding to region 330-364 (SEQ.ID.NO:1) of mature human HRGP.
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3. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 2, said
subfragment having an amino acid length of between 3 and 35 amino acids.
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4. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 3,
having an amino acid length selected from the group consisting of between 3 and 25 amino
acids, 3 and 20 amino acids, 3 and 15 amino acids, 3 and 10 amino acids, and 3 and 8
amino acids.
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5. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment
corresponding to SEQ.ID.NO:18.
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6. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment
corresponding to SEQ.ID.NO:17.
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7. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 6,
wherein said polypeptide comprises an additional glycine (G) residue in the C-terminal end
(residue 26) of said polypeptide, said polypeptide corresponding to SEQ.ID.NO:16.
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8. A substantially pure consecutive and anti-angiogenic polypeptide comprising a subfragment
of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to
SEQ.ID.NO:22.
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9. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 8,
wherein said polypeptide is modified through an acetylation and/or an amidation in the N-
terminal, and/or C-terminal end, said polypeptide corresponding to SEQ.ID.NO:21.
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10. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment
corresponding to SEQ.ID.NO:24.
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11. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 10, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal end, said polypeptide corresponding to SEQ.ID.NO:23.
- 5 12. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to SEQ.ID.NO:26.
- 10 13. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 12, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal ends, said polypeptide corresponding to SEQ.ID.NO:25.
- 15 14. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to SEQ.ID.NO:28.
- 20 15. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 14, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal ends, said polypeptide corresponding to SEQ.ID.NO:27.
16. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, wherein said polypeptide is isolated from human HRGP.
- 25 17. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, wherein said polypeptide is isolated from proteolytically processed human HRGP purified from plasma.
18. A substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-15, wherein said polypeptide is recombinantly produced and/or isolated from recombinantly produced human HRGP.
- 30 19. A synthetically produced, substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-15.
- 35 20. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, characterised in that it does not bind to thrombospondin.
21. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, characterised in that it does not promote angiogenesis.

22. An anti-angiogenic pharmaceutical composition, comprising an effective amount of a substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims.
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23. An anti-angiogenic pharmaceutical composition according to claim 22, further comprising a pharmaceutically acceptable carrier.
24. An anti-angiogenic pharmaceutical composition according to any of claims 22-23, further
10 comprising an anti-angiogenic agent.
25. An anti-angiogenic pharmaceutical composition according to claim 24, wherein said anti-
15 angiogenic agent is selected from the group consisting of angiostatin, thrombostatin,
endostatin, interferon- α , interferon-inducible factor 10, and platelet factor 4.
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26. An anti-angiogenic pharmaceutical composition according to any of claims 22-25, further
comprising an anti-neoplastic agent.
27. An anti-angiogenic pharmaceutical composition according to claim 26, wherein said anti-
20 neoplastic agent is selected from the group consisting of taxol, cyclophosphamide,
carboplatinum, cisplatinum, cisplatin, gancyclovir, camptothecin, paclitaxel, hydroxyurea,
5-azacytidine, 5-aza-2'-deoxycytidine, and suramin.
28. An anti-angiogenic pharmaceutical composition according to any of claims 22-27, further
25 comprising an anti-inflammatory agent.
29. An anti-angiogenic pharmaceutical composition according to claim 28, wherein said anti-
30 inflammatory agent is selected from the group consisting of prednisone, a cox-2 inhibitor,
ibuprofen and aspirin.
30. An anti-angiogenic pharmaceutical composition according to any of claims 22-29, further
comprising an effective amount of Zn²⁺.
31. A substantially pure consecutive and anti-angiogenic polypeptide according to any of claims
35 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for use as a
medicament.
32. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of
40 claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the
manufacture of a medicament for the inhibition of angiogenesis in a mammal.

33. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for treating and/or preventing cancer in a mammal.
- 5 34. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for inhibiting tumour growth in a mammal.
- 10 35. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for treating and/or inhibiting myocardial angiogenesis, diabetic retinopathy, diabetic neovascularization, inappropriate wound healing, or an inflammatory disease in a mammal.
- 15 36. Use according to any of claims 32-35, wherein said mammal is a mouse.
37. Use according to any of claims 32-35, wherein said mammal is a rat.
38. Use according to any of claims 32-35, wherein said mammal is a human.
- 20 39. Method for inhibiting angiogenesis in a mammal, comprising administering a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, to a mammal in need thereof.
- 25 40. An isolated nucleic acid sequence that encodes a consecutive subfragment according to any of claims 1-21.
- 30 41. An expression vector comprising a nucleic acid sequence according to claim 40, optionally operatively linked to a promoter and/or additional regulatory sequences that regulate the expression of said nucleic acid sequence in a eukaryotic or prokaryotic host cell.
42. A host cell transformed and/or transfected with an expression vector according to claim 41.
- 35 43. A host cell according to claim 42, selected from the group consisting of mammalian cells, such as human, mouse or rat cells, and bacteria, yeast, and insect cells.
44. Method for inhibiting angiogenesis in a mammal, comprising administering an isolated nucleic acid according to claim 40, a host cell according to claim 42 or 43 , and/or a vector according to claim 41 to a mammal in need thereof.
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